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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PATTEN, PATRICIA A	

ART UNIT	PAPER NUMBER
1654	9

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,371	BJARNASON, JON BRAGI	
	Examiner	Art Unit	
	Patricia A Patten	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 28-31 and 40-50 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 28-31 and 40-50 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 28-31 and 40-50 are pending in the application.

Election/Restrictions

Arguments with regard to the election of species between the Atlantic cod trypsins I, II and III were considered. In light of the arguments that these trypsins share a 'strong amino acid sequence homology', this aspect of the election requirement has been removed.

Applicant's election of the species arthritis in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 28-31 and 40-50 were examined on the merits.

Drawings

The drawings are objected to because they are unclear (visually). Further, the terms 'Figure 1, 2, ect' have been written in. A proposed drawing correction or

corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Iceland on 06/18/1999. It is noted, however, that applicant has not filed a certified copy of the Icelandic application in this application, nor in the parent application 09/411,688as required by 35 U.S.C. 119(b).

Claim Objections

Claim 43 is objected to because of the following informalities: Claim 43 recites 'with any of trypsin I, trypsin II, trypsin III derived from Atlantic cod'. This should appropriately read 'with any of trypsin I, trypsin II or trypsin III...'. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 43 and 48 are drawn to wherein the trypsin has 'at least 90% amino acid sequence homology with any of trypsin I, trypsin II, trypsin III derived from Atlantic cod'.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or

unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative embodiments. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which can be tolerated in a protein's amino acid sequence and still retain similar biological activity requires a (1) knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which reconserved (i.e., expectantly intolerant to modification), and (2) detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determination to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the real routine of experimentation.

One of the main considerations to be made in determining whether undue experimentation is required is the amount of experimentation required. See In re Wands, 8 USPQ2d 1400 (CAFC 1988). Even if substitutions with natural 20 amino acids encoded by DNA were the only modifications, instant claims would still broadly

encompass a multitude of species; calculated as 20^N * (length)!/N/(length-N)! , wherein "20" is the number of natural amino acids encoded by DNA, "N" is the number of positions where substitutions can occur, "!" is the factorial symbol, "/" is the division symbol and "length" is the total number of amino acids in the protein or peptide. A polypeptide chain of 100 amino acids could exist in 10^{130} combinations.

While recombinant and mutagenic techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar biological activity are limited in any protein/enzyme. The result of such modifications is unpredictable based on the Instant specification. One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g., multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acid modifications in such proteins.

The specification does not support the scope of the claims which encompass all modifications and fragments because the specification does not disclose the following:

a) The amino acid sequence for the claimed protein;

b) The general tolerance to modification and extent of such tolerance;

c) The specific positions and regions of the sequence(s) which can be predictably modified and which regions are critical;

d) What fragments, if any, can be made which retain the biological activity of the intact protein; and

f) The specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, Applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed protein in a manner reasonably correlated with the scope of the claims, broadly including any number of additions, deletions, or substitutions and fragments of any size.

Claims 28-31 and 40-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating some skin conditions as taught in the Instant specification, does not reasonably provide enablement for preventing such conditions, nor does the Specification reasonably provide support for treatment of all the diseases of claim 28 aside from arthritis, tendonitis, phlebitis, psoriasis, acne, eczema, dermatitis and wounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because effective treatments for disease conditions are relatively rare, and may be unbelievable in the absence of strong supporting evidence. Claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments.

To 'prevent' is deemed to mean that the composition of the present invention would in all cases cease the disease from occurring in a patient. The instant specification is lacking any specific working example wherein the compositions of the Instant claims has substantially 'prevented' any disease. Therefore, lacking this guidance, it would require a substantial inventive contribution by one of ordinary skill in the art in order to practice the invention as claimed.

As the state of the art stands, there is no 100% 'cure' or 'prevention' for any of the ailments recited in claim 28. Judging from the prior art, one of ordinary skill in the art *would not have* a reasonable expectation that the composition of the instant claims would essentially 'prevent' skin disorders such as acne. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides

sufficient guidance to permit one to identify those embodiments which are more likely to work that not without actually making and testing them then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that the composition of the Instant claims would essentially and entirely cease diseases such as arthritis, ulcers and wounds. The instant specification does not provide the guidance needed to predictably administer a fish serine proteinase with any reasonable expectation that it would prevent the claimed diseases.

Further, there is no indication within the Instant specification what other diseases could potentially be treated with the compositions of the Instant claims. It appears to be highly speculative that the compositions could in fact treat other diseases besides the ones which were actually demonstrated i.e., arthritis, tendonitis, phlebitis, psoriasis, acne, eczema, dermatitis and wounds. Lacking guidance to the efficacy of the composition with regard to other 'degenerative' ailments, the skilled artisan would be bound to perform undue experimentation without any expectation of success.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, ***he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in***

compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (emphasis added)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28 – 31 and 40-42, 44- 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Faire et al. (US 5,958,406).

de Faire et al. (US 5,958,406) disclosed a method for treating skin conditions such as acne and eczema as well as removing dead or peeling skin (as examples) with

a multifunctional enzyme exhibiting at least one of chymotrypsin, trypsin, collegenase or ellastase activity (which are all serine protease inhibitors) (claim 1, Abstract and col.3, lines 16-33 as examples). de Faire et al. taught that « The enzymes that are substantially structurally similar to the krill-derived multifunctional enzyme have the same utility as the krill enzyme" (col.1, lines 18-20). de Faire et al. further demonstrate in Table 2 that the N-terminal sequence of Atlantic cod serine protease is substantially structurally similar to the krill enzyme n-terminal sequence.

One of ordinary skill in the art would have been motivated to have administered Atlantic cod serine proteases which displayed at least one of a chymotrypsin or trypsin activity to alleviate the symptoms of the claimed diseases, because Atlantic cod serine proteases such as chymotrypsin and trypsin would have acted beneficially in treating aspects of said diseases as clearly taught by de Faire et al. (i.e., col.1, lines 17-29, col.1, lines 32-51 as examples). The ordinary artisan would have reasonably expected that chymotrypsin and trypsin from Atlantic cod, or any other fish would have acted similarly to the krill enzyme which displayed chymotrypsin and/or trypsin activity because chymotrypsins and trypsins are both digestive enzymes with the substantially identical proteinase activity when compared to chymotrypsin and trypsin activity of krill especially lacking convincing evidence to the contrary.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Patricia Patten, whose telephone number is (703) 308-1189. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

September 30, 2003

Patricia Patten

PATRICIA PATTEN
PATENT EXAMINER